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# AN OUTBREAK OF *ESCHERICHIA COLI* O157:H7 INFECTIONS AMONG VISITORS TO A DAIRY FARM

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## ABSTRACT

***Background*** Outbreaks of *Escherichia coli* O157:H7 infections have involved direct transmission from animals and their environment to humans. We describe an outbreak among visitors to a Pennsylvania dairy and petting farm that provides public access to animals.

***Methods*** We conducted both a case–control study among visitors to a farm to identify risk factors for infection and a household survey to determine the rates of diarrheal illness among these visitors. We performed an extensive environmental study to identify sources of *E. coli* O157:H7 on the farm.

***Results*** Fifty-one patients with confirmed or suspected *E. coli* O157:H7 infection were enrolled in the case–control study. The median age of the patients was four years, and the hemolytic–uremic syndrome developed in eight. Contact with calves and their environment was associated with an increased risk of infection, whereas hand washing was protective. The household survey indicated that visitors to the farm during the outbreak had higher than expected rates of diarrhea. Environmental studies showed that 28 of the 216 cattle on the farm (13 percent) were colonized with *E. coli* O157:H7 that had the same distinct pattern on pulsed-field gel electrophoresis that was found in isolates from the patients. This organism was also recovered from surfaces that were accessible to the public.

***Conclusions*** In a large outbreak of *E. coli* O157:H7 infections among visitors to a dairy farm, predominantly children, high rates of carriage of *E. coli* O157:H7 among calves and young cattle most likely resulted in contamination of both the animals' hides and the environment. (N Engl J Med 2002;347:555-60.)



*ESCHERICHIA coli* O157:H7 causes an estimated 60 deaths and 73,000 illnesses annually in the United States.[1] Healthy cattle are the main recognized animal reservoir and may harbor the organism as part of the bowel flora. Most reported outbreaks are due to contaminated food or water.[2] However, direct transmission of *E. coli* O157:H7 from animals and their environment to humans is a growing concern. Most reports are of single cases or small clusters, and few have permitted extensive epidemiologic investigations to establish risk factors for infection.[3-8]

Outbreaks of *E. coli* O157:H7 infection caused by transmission from farm animals or their environment were recognized in the United States during 2000.[9] We describe an outbreak that is notable for two reasons: the number of cases permitted extensive characterization of risk factors, and a concurrent environmental study of the farm was conducted to define sources of infection.

## METHODS

### The Outbreak

During September 2000, an unexpectedly large number of cases of *E. coli* O157:H7 infection occurred in Montgomery County,

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Pennsylvania, and surrounding counties. Officials at the Montgomery County Health Department and the Pennsylvania Department of Health instituted active case finding on September 27. Most patients had been visitors at a popular petting farm in Montgomery County. The farm was a traditional dairy farm that for several decades had hosted visits by the public, especially groups of children, to see and pet the animals. The farm's management estimated that 1500 to 2000 people visited the farm each day. Food and beverages were available at the farm for lunch and snacks. By November 2, 6 patients with the hemolytic–uremic syndrome and 10 patients with diarrhea from Pennsylvania and New Jersey had been reported among farm visitors. The Pennsylvania Department of Health and the Montgomery County Health Department invited the Centers for Disease Control and Prevention (CDC) to assist in the investigation on November 2. The goals of the investigation were to determine the magnitude of the outbreak, to identify risk factors for infection, to interrupt transmission, and to describe the ecology of *E. coli* O157:H7 in the farm environment.

### Epidemiologic Investigation

Surrounding counties and all states were notified of the outbreak. Physicians and medical microbiology laboratories were asked to look for cases associated with the outbreak, to test stools for *E. coli* O157:H7, to report cases to the Montgomery County Health Department, and to forward isolates to state health department laboratories for molecular subtyping.

To develop hypotheses regarding possible sources of *E. coli* O157:H7 infections, investigators selected and interviewed three patients on November 6. They used the CDC standard foodborne-illness hypothesis-generating questionnaire (available at http://www.cdc.gov/ncidod/dbmd/outbreak/stand_qu.htm) with an addendum relating to exposures to animals.

Hypothesis-generating interviews suggested that the outbreak occurred among visitors to the farm. Consequently, a case–control study was conducted among farm visitors to identify specific risk factors for infection.

For case-ascertainment purposes and a case–control study, a probable case was defined as acute diarrhea (three or more loose stools in a 24-hour period) in a person beginning within 10 days after visiting the farm after September 1. A confirmed case was defined as acute diarrhea in a person beginning within 10 days after visiting the farm after September 1, and accompanied by either the hemolytic–uremic syndrome or the isolation of *E. coli* O157:H7 from stool.

Controls were persons who visited the farm after September 1 and did not have diarrhea within 10 days after the visit. Controls were identified by sequential-digit dialing in which patients' telephone numbers were used as a starting point, and all controls were frequency-matched to the patients according to age group (less than 1 year, 1 to 4 years, 5 to 8 years, 9 to 12 years, 13 to 20 years, and 21 years or older). One person per household was included. The goal was to obtain two controls per patient.

A questionnaire was developed that focused on exposures to animals, food and beverages consumed at the farm, and hand-washing practices. The questionnaire was administered by telephone from November 12 through 19. Patients and controls were asked about the dates of their visit to the farm, contact with animals and their environment, foods and beverages consumed, and hand washing and other behavior at the farm. Patients were also asked about their clinical history. When a patient or control was 15 years of age or younger, the interview was conducted with the parent or guardian who had been present during the visit to the farm.

To estimate the rate of illness among petting-farm visitors, a household survey was conducted during the selection of controls for the case–control study. Members of contacted households were asked whether they had visited the farm and those who had were queried about any history of acute diarrhea in the 10 days after the visit.

### Environmental Investigation

The layout of the farm was determined, and a complete list of food and beverages available to visitors was compiled. A census of the animals present at the farm during September and October was conducted. The farm's entire population of domestic animals was subjected to rectal- or cloacal-swab sampling between November 13 and 16. Samples were cultured for *E. coli* O157:H7 and subtyped with the use of pulsed-field gel electrophoresis (PFGE).

Swabs of the railings around animal enclosures were obtained. Water samples were collected at sites around the farm. Biofilm samples were collected from watering troughs. All samples were cultured for *E. coli* O157:H7 and subtyped with the use of PFGE.

### Laboratory Investigation

Human fecal samples and biofilm samples from watering troughs were plated on sorbitol–MacConkey agar after immunomagnetic separation. Rectal and cloacal swabs from animals and water samples were plated on sorbitol–MacConkey agar. Immediately after collection, all swab samples were placed in Carey–Blair transport medium and were cultured within 48 hours. Isolates of *E. coli* O157:H7 were confirmed serologically and tested for toxin production with the use of an enzyme immunoassay at the Pennsylvania State Public Health Laboratory. Environmental-surface swabs were forwarded to the CDC for culture for *E. coli* O157:H7. Molecular subtyping of all *E. coli* O157:H7 isolates was performed at the Virginia State Public Health Laboratory, the Pennsylvania State Public Health Laboratory, and the CDC with the use of standard methods of PFGE.[10,11] Shiga toxin genes were detected by multiplex polymerase chain reaction with the use of established primers.[12]

### Statistical Analysis

Statistical analyses were conducted with the use of Epi Info, version 6.04 (CDC), SAS System for Windows, release 8.0 (SAS Institute), and LogXact for Windows, version 4.1 (Cytel Software). A multivariate logistic-regression model was built from the set of measured quantities to identify independent variables that were significant risk factors for infection. Factors considered for inclusion in the final model were demographic variables, direct contact with animals, environmental exposures, hand–mouth activities, foods and beverages, and hand-washing behavior. Where appropriate, combined exposure variables were defined. The analysis was stratified according to age to account for differences in exposure that might have been the result of age.

## RESULTS

### Epidemiologic and Clinical Information

As of November 12, 2000, 15 confirmed cases and 36 probable cases of *E. coli* O157:H7 had been identified. Patients were from five counties in eastern Pennsylvania and one county in New Jersey. No residents or employees of the farm reported having diarrhea during the outbreak period. Of the 51 patients, 25 (49 percent) were female. They ranged in age from 1 through 52 years (median, 4), and 47 (92 percent) were 10 years of age or younger. Dates of onset could be accurately determined for 49 patients and ranged from September 4 through November 8, 2000 (Fig. 1). Patients reported having bloody diarrhea (37 percent), fever (45 percent), and vomiting (45 percent). Sixteen patients (31 percent) were hospitalized. The hemolytic–uremic syndrome developed in eight patients (16 percent), all of whom were 10 years old or

younger. End-stage renal failure developed in one of these eight patients, and renal transplantation was required. No patient died. Within days after the farm and public health officials prohibited public access to animals on November 4, no further cases were reported (Fig. 1).

Univariate analysis showed that patients were more likely than controls to have had direct contact with calves (e.g., petting) and their environment (e.g., touching railings or having contact with manure) at the farm (Table 1). Among children who were five to eight years of age, the estimated duration of exposure to cattle was significantly longer among patients than among controls (mean, 19.3 vs. 8.2 minutes; $P=0.005$). Contact with any animal (e.g., llamas, sheep, goats, or pigs) was also more common among patients than controls. The frequency of markers of hand–mouth activity, including nail biting and purchasing food or drink from an outdoor concession at the farm, was greater among patients than controls. Visitors who washed their hands in the sink were less likely to become ill, indicating a protective effect of hand washing (Table 1).

On multivariate logistic-regression analysis, viewing calves less than 6 weeks of age (odds ratio, 3.9; 95 percent confidence interval, 1.1 to 17.3; $P=0.027$) and viewing calves 6 to 35 weeks of age (odds ratio, 3.3; 95 percent confidence interval, 1.3 to 8.8; $P=0.007$) remained significant risk factors for infection, and hand washing approached significance for protection (odds ratio, 0.5; 95 percent confidence interval, 0.2 to 1.1; $P=0.081$) (Table 2).

In the process of obtaining controls, we called 19,698 telephone numbers in Montgomery County and surrounding counties. Of the 3497 households contacted, 134 (4 percent) reported that a household member had visited the farm after September 1. Of these, 22 (16 percent) reported that the household member had had diarrhea during the 10 days after the visit. The expected rate of diarrhea in the general population is 7 percent per 10 days (FoodNet Population Survey, CDC: unpublished data, 1998–1999).

#### Environmental Investigation

The farm was a small, working dairy farm. Calves younger than 6 weeks of age were kept in hutches, and calves 6 to 35 weeks of age were kept in a barn. Both areas were fully accessible to the public. Heifers and mature cows were kept separate from the calves and were less accessible to the public. In addition, pigs, donkeys, llamas, sheep, goats, peafowl, chickens, cats, and dogs were displayed. A store and concession stands sold food and drink that could be consumed in the animal areas. Raw milk was not served. Hand-washing facilities were limited, not configured for use by children, and unsupervised.

Thirty-three of 216 cattle (15 percent) were colonized with *E. coli* O157:H7. Of these, 28 of 33 (85 percent) were colonized with *E. coli* O157:H7 that had the same PFGE pattern as isolates recovered from farm visitors who became ill (Table 3). Overall, calves and heifers were more often colonized than older cattle. Of calves less than six weeks of age, 3 of 13 (23 percent) were colonized with *E. coli* O157:H7; 2 of 3 isolates (67 percent) had the same PFGE pattern as the isolates from the outbreak. Of calves 6 to 35 weeks of age, 5 of 38 (13 percent) were colonized with *E. coli* O157:H7, all 5 of which had the same PFGE pattern as the isolates from the outbreak. Of small heifers, 10 of 25 (40 percent) were colonized with *E. coli* O157:H7; 9 of 10 isolates (90 percent) had the same PFGE pattern as the isolates from the outbreak. Of large heifers and dry cows, 11 of 40 (28 percent) were colonized with *E. coli* O157:H7;

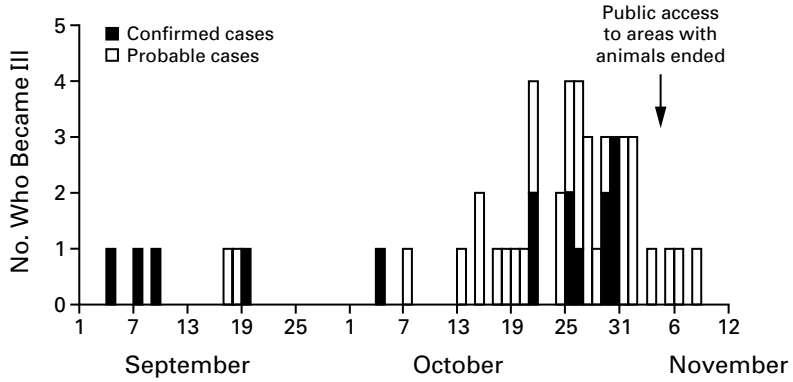


**Figure 1.** Onset of Diarrheal Illness among 49 Visitors to a Pennsylvania Farm, September to November 2000.

**TABLE 1.** UNIVARIATE ANALYSIS OF RISK FACTORS FOR *ESCHERICHIA COLI* INFECTION AMONG FARM VISITORS.

| CATEGORY | SUMMARY ODDS RATIO (95% CI)* | P VALUE |
|---|---|---|
| Exposure to animals or their environment | | |
| Viewing cattle or calves | 10.9 (1.7–70.7) | 0.012 |
| Viewing calves <6 wk old | 4.7 (1.6–13.6) | 0.004 |
| Viewing calves 6–35 wk old | 3.8 (1.7–8.5) | 0.001 |
| Touching calf-hutch fence | 3.8 (1.5–9.7) | 0.007 |
| Contact with cattle manure | 2.5 (1.2–5.2) | 0.013 |
| Direct contact with animals | | |
| Touching any animal | 4.5 (1.8–11.0) | 0.001 |
| Touching any calf | 2.3 (1.1–4.7) | 0.021 |
| Hand–mouth activities | | |
| Purchasing food or drink at farm† | 3.0 (1.4–6.1) | 0.003 |
| Nail biting | 2.5 (1.1–5.7) | 0.037 |
| Hand-washing behaviors | | |
| Washing hands in sink | 0.19 (0.04–0.94) | 0.042 |
| Washing hands before eating | 0.23 (0.08–0.74) | 0.013 |
| Washing hands after touching animals | 0.27 (0.09–0.86) | 0.027 |
| Other behaviors | | |
| Watching cattle through glass window | 0.15 (0.03–0.75) | 0.021 |

*CI denotes confidence interval.

†No individual food or drink item reached statistical significance by multivariate analysis.

**TABLE 2.** MULTIVARIATE ANALYSIS OF EXPOSURES AMONG PATIENTS AND CONTROLS VISITING THE FARM.

| EXPOSURE | PATIENTS | CONTROLS | ODDS RATIO (95% CI)* |
|---|---|---|---|
| | no./total no. (%) | | |
| Viewing calves | | | |
| <6 wk old | 47/51 (92) | 63/91 (69) | 3.9 (1.1–17.3) |
| 6–35 wk old | 41/51 (80) | 47/91 (52) | 3.3 (1.3–8.8) |
| Hand washing | 3/20 (15) | 18/40 (45) | 0.5 (0.2–1.1) |

*Adjusted odds ratios (conditional logistic-regression analyses) were stratified according to age group. CI denotes confidence interval.

8 of 11 (73 percent) had the same PFGE pattern as the isolates from the outbreak. Of nine "pre-fresh" cows (cows that were within two weeks before parturition), one (11 percent) was colonized with *E. coli* O157:H7; the isolate had the same PFGE pattern as the isolates from the outbreak. Of 91 lactating cows, 3 (3 percent) were colonized with *E. coli* O157:H7, and each isolate had the same PFGE pattern as the isolates from the outbreak.

One of 7 biofilm samples (from a watering trough in a calf hutch) and 1 of 37 surface swabs (from the lower railing of the heifer-area fence) yielded *E. coli* O157:H7. PFGE of the isolate from the heifer-area railing, but not the biofilm isolate, matched the pattern obtained on PFGE of isolates from the patients. None of the seven water samples from the farm yielded *E. coli* O157:H7 (Table 3).

**TABLE 3.** SOURCES OF *ESCHERICHIA COLI* O157:H7 AND PATTERN OF ISOLATES ON PULSED-FIELD GEL ELECTROPHORESIS (PFGE).*

| SOURCE | *E. COLI* O157:H7 ISOLATES | PFGE PATTERN |
|---|---|---|
| | no./total no. (%) | |
| Patients | 8/51 (16) | 8/8 (100) |
| All cattle | 33/216 (15) | 28/33 (85) |
| Calves <6 wk old | 3/13 (23) | 2/3 (67) |
| Calves 6–35 wk old | 5/38 (13) | 5/5 (100) |
| Small heifers | 10/25 (40) | 9/10 (90) |
| Large heifers and dry cows | 11/40 (28) | 8/11 (73) |
| "Pre-fresh" cows (within 2 wk before parturition) | 1/9 (11) | 1/1 (100) |
| Lactating cows | 3/91 (3) | 3/3 (100) |
| Animals other than cattle | 0/43 | NA |
| Railings around animal enclosures | 1/37 (3) | 1/1 (100) |
| Biofilm samples from watering troughs | 1/7 (14) | 0/1 |
| Water | 0/7 | NA |

*NA denotes not applicable.

### Laboratory Results

The number of isolates of *E. coli* O157:H7 and the results of molecular subtyping are summarized in Table 3. All 8 *E. coli* O157:H7 isolates from patients and 29 (83 percent) of 35 isolates from nonhuman sources had the same rare PFGE pattern (EXHX01.0070, pattern 70) and produced both Shiga toxin 1 and Shiga toxin 2.

## DISCUSSION

We describe a large outbreak of *E. coli* O157:H7 infections that were directly transmitted from animals and their environment to people, largely children. Contact with calves up to 35 weeks old and their environment was associated with illness. Among all farm visitors, the data showed a trend toward hand washing as providing protection.

The proportion of cattle colonized with *E. coli* O157:H7 at the farm (15 percent) was higher than in other studies of cattle herds (rates are typically in the range of less than 0.5 percent to 2 percent).[13,14] High rates of colonization occur among young cattle, and occasionally, periodic, sharp fluctuations in prevalence, to rates above 10 percent, have been identified.[15] Determinants of the rates of *E. coli* O157:H7 colonization in cattle herds are not yet well understood.[15,16] Collection and transport of samples and culture methods may affect the rates. Although some

investigators have sampled fresh fecal pats,[13] our use of rectal swabbing was consistent with the methods of other studies.[14] Had we used immunomagnetic separation for the rectal swabs obtained from animals, as we did for the human fecal specimens, the isolation rate would probably have been even higher.[17] The high rate of colonization of cattle may indicate that the *E. coli* O157:H7 strain involved in the outbreak had recently been introduced to the farm, leading to the peak in prevalence that may occur when a new strain sweeps through a previously unexposed herd.[15] The high prevalence of *E. coli* O157:H7 colonization in the herd at the farm most likely contributed to increased contamination of cattle hides and the environment during the outbreak period. This increased contamination in turn created greater risk to farm visitors than might have occurred had the colonization rate of cattle been lower. Despite this, farm workers reported no diarrheal illness during the outbreak period. This finding is consistent with studies showing that previous infection and frequent reexposure to *E. coli* O157:H7 may confer some protection against symptomatic infection.[18-20]

Evidence from a household survey suggests that higher than expected rates of diarrhea occurred among visitors to the farm, indicating excess illness that was not identified by routine case finding. This highlights the potential scale of zoonotic outbreaks of *E. coli* O157:H7 infection and suggests that the importance of this mode of transmission may previously have been underestimated. It also underscores the risk associated with bringing children, a group at increased risk for severe illness due to *E. coli* O157:H7 infection, together with cattle, major reservoirs of *E. coli* O157:H7, in an uncontrolled environment where eating is encouraged and hand-washing facilities are inadequate. The outbreak at the farm may not be an isolated event. A case–control study conducted by the Foodborne Diseases Active Surveillance Network (FoodNet) of the CDC during 1996 and 1997 found that living on or visiting a farm with cows during the seven days before illness was associated with an increased risk of sporadic *E. coli* O157:H7 infection.[21] Studies in other countries have found similar associations.[22,23] Two random-digit-dialing telephone surveys of approximately 9000 persons each, conducted by FoodNet during 1996–1997 and 1998–1999, showed that 2 percent of respondents reported visiting a petting zoo in the five to seven days before the interview,[24,25] indicating that the population at risk is large. Furthermore, settings such as agricultural fairs attract large numbers of visitors and create conditions similar to those found at the farm.[8]

*E. coli* O157:H7 can survive in the environment for months[26-28] and thus pose an ongoing source of infection of humans, even in the absence of direct contact with animals. The frequency of *E. coli* O157:H7 in U.S. cattle herds combined with the environmental persistence of the organism supports the recommendations that all cattle should be handled as if they are colonized and that all cattle environments should be approached as if they were contaminated with *E. coli* O157:H7.

Farm environments can be made safer for visitors. Prevention strategies were developed to help reduce the risk of transmission of enteric pathogens at petting zoos, farms open to the public, animal exhibits, and other venues where the public has contact with farm animals.[9] The strategies include the use of hand washing, controlled and supervised contact with animals, and clear separation of food-related activities from areas housing animals.

Evidence is growing that contact with farm animals and their environment is a substantial contributor to the risk of *E. coli* O157:H7 infection. This outbreak underscores the need to consider zoonotic transmission during searches for the source of *E. coli* O157:H7 and other enteric infection and that simple measures such as effective hand washing can make contact with farm animals and their environments safer.

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